

REMARKS

This *Response* is filed in reply to the non-final *Office Action* mailed on 2 September 2011. Claims 10, 16-18, 50, 51, 53-55, 64, 65, 67-69, 71, 72, 74, 76, 77, 79-82, 84-87, 89-92, 95-98, 100, 102-106, and 108-11 are currently pending and stand rejected under 35 U.S.C. §§102(e)/103(a). Claims 17, 54, 68, 79, 80, 90, 91, 96, 97, 105, 106 and 108-111 stand further rejected under 35 U.S.C. §112, second paragraph. In response, Applicants amend Claims 108-111, and respectfully traverse the other rejections.

Applicants submit this *Response* solely to facilitate prosecution. As such, Applicants reserve the right to pursue claims of broader or similar scope as originally filed in a continuation application or other application after allowance of the present Application. Applicants do not concede that any current or past rejections are correct and reserve the right to challenge such rejections later in prosecution or on appeal. Accordingly, any amendment, argument, or claim cancellation is not to be construed as abandonment or disclaimer of subject matter. As certain of the current amendments may include broadening amendments, Applicants respectfully request the Examiner to revisit any previously reviewed references cited in this Application to further ensure that the currently pending claims remain patentable over any previously reviewed references.

I. Objection to *Abstract*

In the *Office Action*, the Examiner raises for the first time an objection to the current *Abstract* of the disclosure, alleging that it does not refer to the claimed subject matter, requesting a correction, and citing to MPEP §608.01(b). Applicants respectfully disagree with this objection. The *Abstract* should be directed to the **technical disclosure** of the *Application*. Neither 37 C.F.R. nor the MPEP require that the *Abstract* align itself with the claimed subject matter. 37 C.F.R. §1.72 states clearly that the “purpose of the abstract is to enable the United States Patent and Trademark Office and the public generally to determine quickly from a cursory inspection the **nature and gist of the technical disclosure**.” MPEP 608.01(b), cited by the Examiner, actually reinforces this point: “The Examiner in the first *Office action* should require the submission of an abstract **directed to the technical disclosure** in the specification.” There is no requirement that the *Abstract* be modified to align itself with the specific claims of a specific family member of the patent application family. The current *Abstract* properly reflects the

contents of the **disclosure** of the *Application*, and as a result meets the requirements of 37 C.F.R. §1.72 and MPEP §608.01(b). For this reason, the objection should be withdrawn.

II. Claim Rejections under §112, ¶2 are improper and should be withdrawn

In the *Office Action*, Claims 17, 54, 68, 79, 80, 90, 91, 96, 97, 105, 106 and 108-111 are rejected under §112, second paragraph, for failing to particularly point out and distinctly claim the subject matter that the Applicants regard as the invention. In particular, Claims 17, 54, 68, 76, and 97 are allegedly indefinite for use of the term “comprises,” apparently in conjunction with the term “fluorescent property.” Claims 85-87 are allegedly indefinite for the use of the term “comprises,” apparently in conjunction with the ‘recited groups’ in those claims. Claims 79, 80, 81, 90, 91, 105, and 106 are allegedly indefinite for the term “about.” Claims 10, 50, 64, 71, 79 and 89 are allegedly indefinite for the term “change” as it relates to “change” in a “fluorescent property.” Claims 108-111 are allegedly indefinite for the terms “a native polymerase,” “involved,” and “cysteine residue replacement.” Applicants amend Claims 108-111, and respectfully disagree with the other rejection for the reasons set forth below.

Applicant notes that claims comply with the requirement for definiteness if “the claim meets the threshold requirements of clarity and precision, [regardless of] whether more suitable language or modes of expression are available.” MPEP §2173.02. The definiteness is analyzed not in a vacuum but in light of the content of the application’s disclosure, the teachings of the prior art, and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. *Id.* The claim as a whole should be considered when determining whether it apprises one of ordinary skill of its scope. *Id.* Moreover, unless the patentee is acting as its own lexicographer, the claims should be given their ordinary and customary meaning as understood by one of ordinary skill in the art at the time of the invention. MPEP§2111.01 (citing *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (*en banc.*))

The Examiner improperly rejects the claim term “fluorescent property” in combination with “comprises” in Claims 17, 54, 68, 76, and 97. One of ordinary skill will recognize that fluorescent groups will display a number of fluorescent properties. The language in Claims 17, 54, 68, 76, and 97 require that the fluorescent property include a duration, intensity and/or frequency of emitted fluorescent light. Nothing within that term would be indefinite to one of ordinary skill in the art.

The Examiner improperly rejects the term “comprises” in Claims 85-87, although the Examiner only points to ‘recited groups’ without specifying what the recite group is. Applicants note that the term “comprises” is used in conjunction with three different terms in the three claims. Claim 85 contains “each of the nucleotides comprises dNTPs,” which is clearly a term known to one of ordinary skill. Claim 86 has the same language as Claims 17, 54, 68, 76, and 97 above. In Claim 87, “comprises” is used with fluorescent tag, donor, and acceptor, none of which are indefinite to one of ordinary skill.

The Examiner improperly rejects Claims 10, 50, 64, 71, 79 and 89 for the term “change” as it relates to “change” in a “fluorescent property.” Applicants submit that one of ordinary skill would understand “change” of a “fluorescent property” to mean that a tag with a fluorescent property will exhibit a different state for the fluorescent property. By way of example, a fluorescent property might be the intensity of light, and a change could indicate different light intensities under certain conditions. One of ordinary skill would understand what the “change” of fluorescent property could entail, and therefore the claim term is not indefinite.

The Examiner improperly rejects Claims 79, 80, 81, 90, 91, 105, and 106 as indefinite for the term “about.” Applicant submits that this rejection is improper under at least MPEP§2173.05(b), as specifically cited by the Examiner in the Office Action. In particular, the Federal Circuit recognized that “about” was definite when it could be clearly assessed by a stopwatch. MPEP§2173.05(b), (citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, (Fed. Cir. 1983.)) In the same manner, “about” is used for a distance measured in angstroms in each of the cited claims. Moreover, MPEP§2173.05(b) states clearly that claims reciting “at least about” are invalid **where there is close prior art**. However, no cited art raises this issue. Relative terminology is acceptable when one of ordinary skill would understand what is claimed. In this instance, one of ordinary skill will understand what “about X angstroms” would mean.

The Examiner improperly rejects Claims 108-111 for the terms “native polymerase,” “involved,” and “cysteine residue replacement.” Applicants submit that one of ordinary skill in the art would recognize that a “native polymerase” is a polymerase isolated from a native source, as opposed to a recombinant or modified polymerase. One of ordinary skill would recognize that “not involved in the functioning of the polymerase” would mean that a modification that does not destroy the functioning of the polymerase. One of ordinary skill would understand that

“cysteine” is an amino acid, it is a “residue” in a poly-amino acid molecule, also called a peptide, and that methods of modifying native peptides often involve making a “replacement” of one or more residues in the chain. Hence, “cysteine residue replacement” would not be indefinite to one of ordinary skill in the art. Applicants also note that cysteine replacement is described within the application at least at [0216], [0231], and [0300]-[0301].

The Examiner also rejects Claims 108-111 for a polymerase that is “native” which has also undergone mutation. Applicants note that this statement implies that the Examiner understands, and therefore one of ordinary skill in the art would also understand, what the allegedly indefinite terms in Claims 108-111 actually mean, which further supports that they are not indefinite. Applicants do not agree with the Examiner’s rejection, but do offer an amendment to further clarify the language in Claims 108-111, changing “including” to “with” to further clarify the claim invention.

For at least the reasons set forth above, Applicants submit that Claims 17, 54, 68, 79, 80, 90, 91, 96, 97, 105, 106 and 108-111 are not indefinite under §112, second paragraph. Applicants respectfully request that the rejections be withdrawn.

III. Claim Rejections under §§102(e)/103(a) are improper and should be withdrawn

In the *Office Action*, Claims 10, 16-18, 50, 51, 53-55, 64, 65, 67-69, 71, 72, 74, 76, 77, 79-82, 84-87, 89-92, 95-98, 100, 102-106, and 108-11 are rejected under §102(e) as anticipated by or, in the alternative, under §103(a) as obvious over U.S. Patent 7,033,764 (hereinafter “Korlach.”) Applicants respectfully disagree for at least the following reasons.

A. Korlach does not anticipate the claimed invention

To anticipate under §102, a reference “must not only disclose all elements within the four corners of the document, *but must also disclose those elements arranged as in the claim.*” *Net MoneyIn, Inc. v. Verisign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008). “Thus, it is not enough that the prior art reference discloses part of the claimed invention, which an ordinary artisan might supplement to make the whole, or that it includes multiple, distinct teachings that the artisan might somehow combine to achieve the claimed invention.” *Id.* at 1371. The anticipatory reference must contain “all the limitations of the claims arranged or combined in the same way as the recited claims.” *Id.* At 1370.

Korlach does not teach, either explicitly or impliedly, a composition having a polymerase with a polymerase tag covalently bonded to a site on the polymerase and nucleotide or analog

types for the polymerase, at least one nucleotide or analog type that includes a nucleotide tag bonded to a part of the nucleotide that is released due to action of the polymerase as the nucleotide is being incorporated, with at least one of the tags having a fluorescence property that changes during each incorporation due to an interaction between the polymerase and the nucleotide, and the polymerase lacking the ability to remove a previously incorporated nucleotide, as exemplified by Claim 10. The Examiner does not point to any section of Korlach with “all the limitations of the claims arranged or combined in the same way as the recited claims” as required by *Net MoneyIn*, and therefore Korlach cannot anticipate.

Specifically, the Examiner’s reliance on Col. 26 for the §102(e) rejection of the Claims is improper for either of two possible reasons. First, Col. 26 cannot be relied upon to disclose a tag on the nucleotide that is cleavable. The entirety of the disclosure in Col. 26 is directed to the use of FRET to lower the background fluorescence in the growing nucleotide chain **due to the incorporation of fluorescent groups in previous nucleotides**. Korlach, col. 26, ln. 9-34. Korlach specifically recites this contention in the opening topic sentence of the paragraph: “Detection of FRET ... suggests a further elegant possibility of lowering **background from incorporated nucleotides**.” *Id.*, col. 26, ln. 9-14. Korlach repeats this description further in the paragraph as well, stating, “**Already incorporated nucleotides** farther away from the donor would not contribute to the fluorescent signal...” *Id.*, col. 26, ln19-21. The disclosure in Col. 26 does not teach or suggest a cleavage fluorescent group in combination with FRET, and a §102(e) rejection that relies on such a conclusion is improper.

Second, if the Examiner alternatively relies on Col. 26 only for the concept of FRET with a fluorescent donor on the polymerase and a fluorescent acceptor on the nucleotide and disregards the remaining portions of that paragraph, then the rejection is improper as a rejection under §102(e) for anticipation because it violates the instructions in *Net MoneyIn*. The element that the Examiner seems to rely on in this alternative argument is taken out of context from the disclosure, and is cobbled together with other selective portions of Korlach to present the rejection. Such an argument contradicts the rule created by the Federal Circuit that “it is not enough that the prior art reference discloses part of the claimed invention, which an ordinary artisan might supplement to make the whole, or that it includes multiple, distinct teachings that the artisan might somehow combine to achieve the claimed invention.” *Net MoneyIn* at 1371. The elements must be combined as recited in the claims.

The anticipatory reference must contain “all the limitations of the claims **arranged or combined in the same way as the recited claims.**” *Id.* at 1370 (emphasis added.) Neither reasoning based on Col. 26 satisfies this instruction. For at least the reasons set forth above, Applicants submit that the rejections of pending Claims 10, 16-18, 50, 51, 53-55, 64, 65, 67-69, 71, 72, 74, 76, 77, 79-82, 84-87, 89-92, 95-98, 100, 102-106, and 108-11 as anticipated under §102(e) by Korlach are improper and respectfully request that the rejections be withdrawn.

B. Korlach does not make obvious the claimed invention

In order to reject a claimed invention as obvious, the *prima facie* case of obviousness, as stated in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) and reiterated in *KSR*, must be shown: Determine the scope and content of the prior art; ascertain the differences between the claimed invention and the prior art; and resolve the level of ordinary skill in the art. MPEP §2141. These determinations must be made based on the level of understanding “at the time the invention was made.” *Id.*, citing 35 U.S.C. §103(a). Applicants assert that the second prong, ascertaining the difference between the claimed invention and the prior art, fails because Korlach demonstrates a problem in the art that the claimed invention solves.

The disclosure in Korlach at Col. 26, ln. 9-34 describes a problem that the prior art reference fails to solve. Korlach struggles to deal with fluorescence from nucleotides containing fluorescent groups already present in the growing nucleic acid, and Korlach tries to overcome that problem by relying on FRET that will only reach the nearest fluorescent acceptor on the incoming nucleotide. This FRET technique in Korlach also must be combined with photobleaching or photochemical cleavage in order to achieve a good response. Korlach, Col. 26, ln. 29-31. In contrast, Applicants’ claimed invention solves this problem by removing the acceptor group from the growing nucleotide chain, and thereby solves a problem that Korlach attempted to address with more complicated methods.

For at least the reasons set forth above, Applicants respectfully submit the pending Claims are non-obvious over the cited art. Applicants respectfully submit the Examiner has not presented a *prima facie* case of obviousness in view of the above, and respectfully requests that the rejection be withdrawn

C. Korlach does not disclose or make obvious the limitations of Claims 108-111.

In order for a reference to be prior art, it must disclose or make obvious each and every aspect of the claimed invention. In addition to the reasons provided above, Korlach does not

teach or suggest the elements present in Claims 108-111. Specifically, nowhere within Korlach is a discussion of cysteine residue replacement in order to incorporate the polymerase tag to the modified polymerase. Korlach provides no discussion of replacements, no discussion of cysteine, and only a single mention of a donor on a polymerase in Col. 26. Moreover, the description of the donor on the polymerase in Col. 26 fails to provide any enablement or context of how the donor is attached, and provides no evidence for a cysteine replacement strategy in a native polymerase.

The Examiner also suggests that Claims 108-111 are a product-by-process claim. Applicants submit that this construction is inapplicable to the instant claims. Nothing in Claims 108-111 describe the process for preparing a compound, nor a compound prepared by a process involving a series of steps.

Applicants also note that the Examiner's circular logic in paragraph 25 of the Office Action is improper. The Examiner alleges that polymerases in Korlach encompasses the claimed polymerases, the polymerases in Korlach allegedly have the properties of the claimed polymerases, and therefore that the claimed polymerases are anticipated by the polymerases in Korlach. However, the final conclusion and the first evidentiary statement in the logic chain are the same, effectively making the argument circular. Korlach does not teach or suggest cysteine residue replacements in native peptide as means for incorporating a donor tag into the polymerase. For that reason, Korlach cannot teach or suggest the claimed invention.

For at least the reasons set forth above, Applicants respectfully submit the pending Claims are novel and non-obvious over the cited art. Applicants respectfully submit the Examiner has not presented a *prima facie* case of obviousness in view of the above, and respectfully requests that the rejection be withdrawn.

CONCLUSION

By the present *Response*, Applicants assert that this *Application* has been placed in full condition for allowance. Accordingly, Applicants respectfully request early and favorable action. The fee for a three month extension of time of \$1270 is filed herewith. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any fees that may be required, or credit any overpayment, to Deposit Account No. 20-1507. Should the Examiner have any further questions or reservation, the Examiner is invited to telephone the undersigned at (404) 885-2708.

Respectfully submitted,

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